

Curating a Minimal Set of Reaction Rules to Cover The Entire Space of Common Enzymatic Transformations

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Introduction

Metabolic In-silico Network Expansion (MINE) Database

Enzyme-substrate promiscuity is the ability for enzymes to catalyze the same general enzymatic transformation on a broad range of non-native metabolites.

The ability to predict these enzymatic side reactions has significant implications for metabolic engineering, which allows for 1) harnessing novel biosynthetic capabilities of enzymes, and 2) elucidating underground metabolic networks in microbes.

The goal of the MINE database is: **providing a freely accessible tool and developer-friendly API that utilizes knowledge of enzyme promiscuity to construct an extended metabolite database.**

Metabolic In Silico Network Expansion Databases

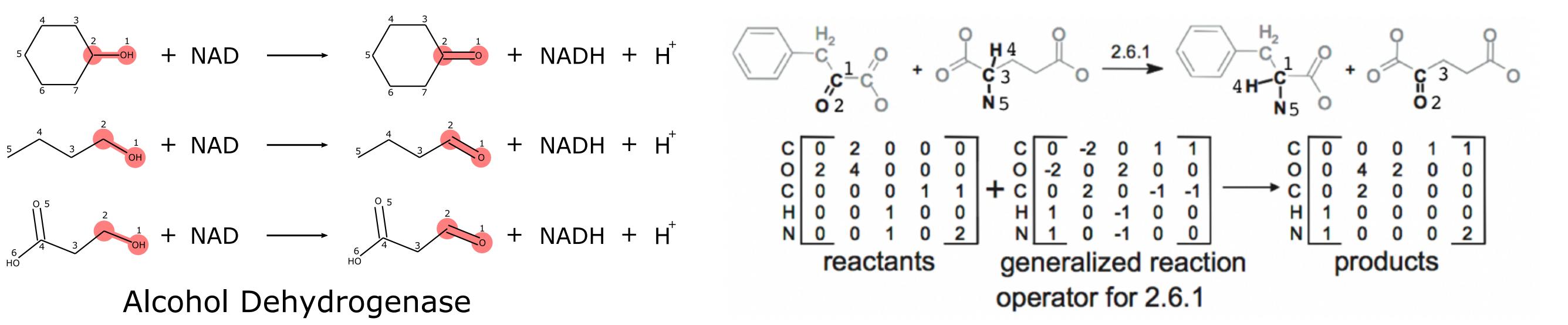


Welcome to the home of the MINE databases. These databases expand the known metabolome using the BNICE framework with hand-curated reaction rules. If it's your first time on the website, we recommend taking one of the tours below. Access to the database is also possible through a REST API. Please contact us for the latest versions.

minedatabase.ci.northwestern.edu

Enzyme-Substrate Promiscuity

Enzymatic Reaction Rules for Retrobiosynthesis



2. Formulating Reaction Rules that Can Capture and Apply Enzymatic Transformation Patterns

1. Capturing Enzymatic Reaction Patterns from Atom-Mapped Metabolic Reactions
2. Generating an Enzymatic Reaction Network to Identify Novel Pathways

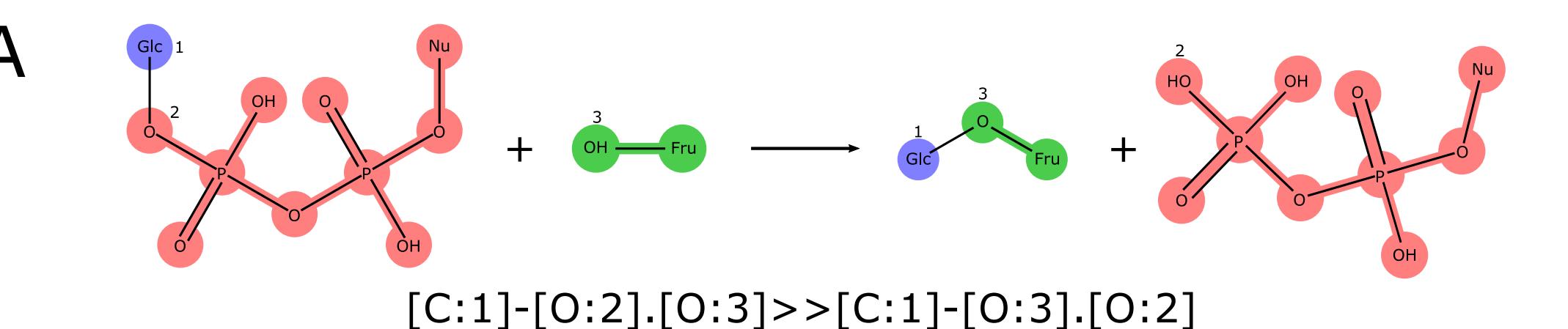


Curation of Enzymatic Reaction Rules

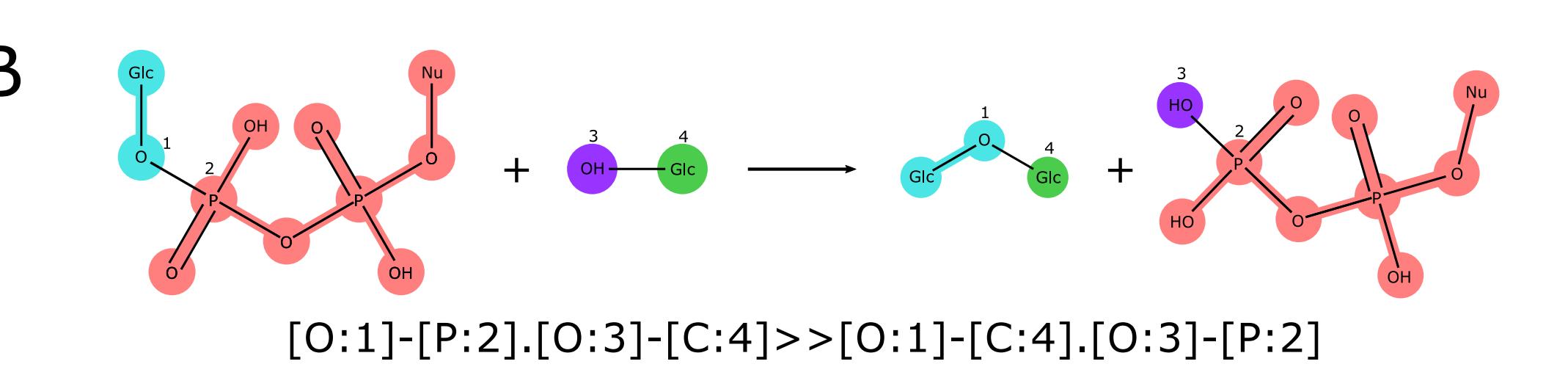
A Minimal Set of Rules to Cover All Enzymatic Reactions?

- 1) Rules describe atoms directly involved in bond changes.
- 2) Each rule represents a unique metabolic transformation.
- 3) Rules comprehensively cover common enzymatic reactions.

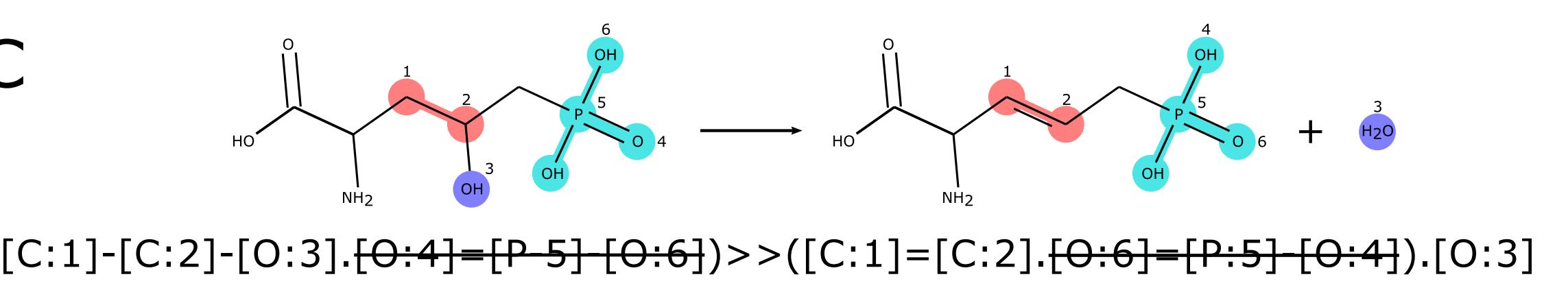
Inconsistent Atom-mappings Complicate Rule Generation



Correct Reaction Rule Abstracted from 2.4.1.13

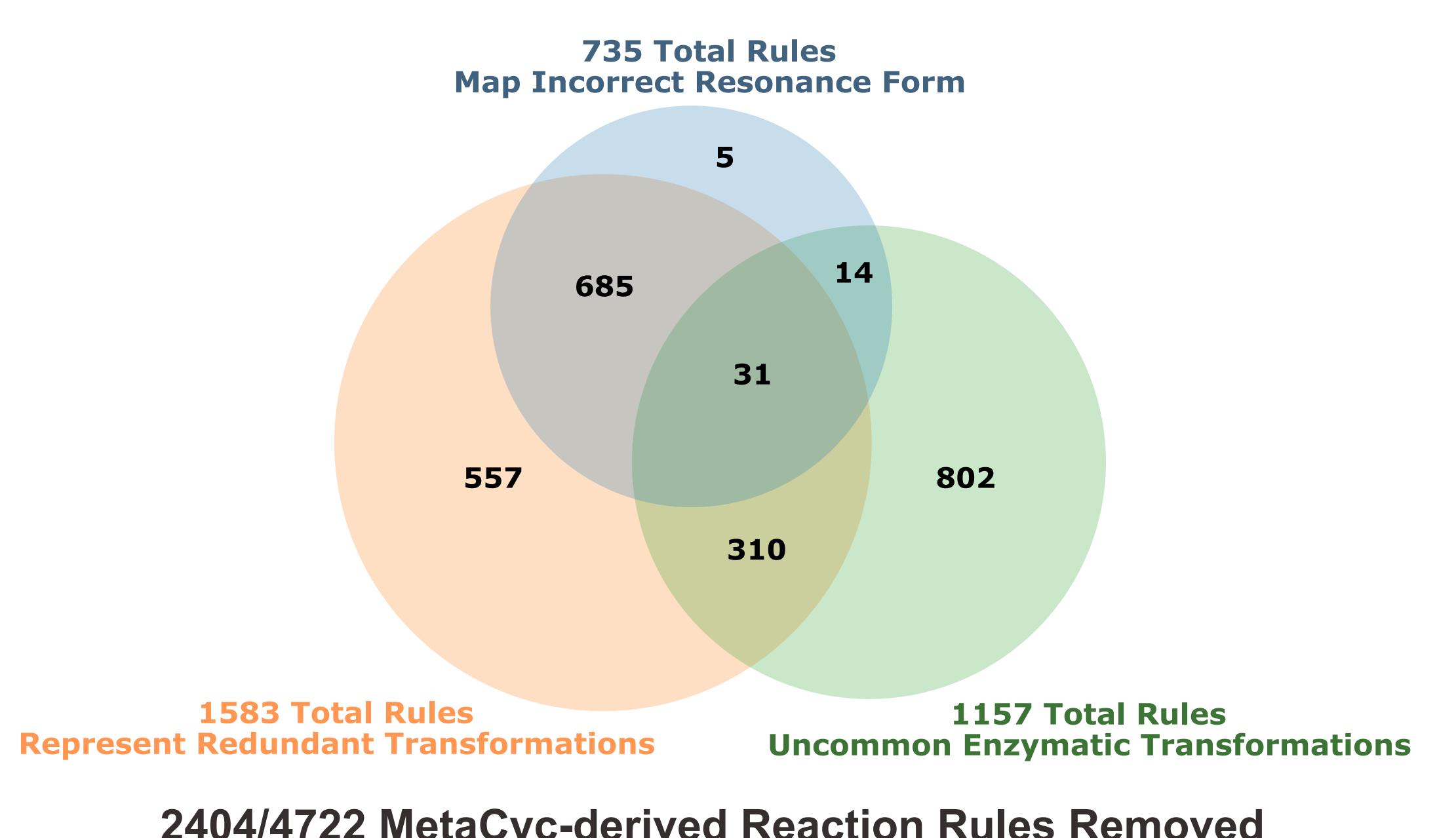


Redundant Reaction Rule Abstracted from 2.4.1.245 Due to Atom-Mapping Inconsistency



Incorrect Reaction Rule Abstracted from 4.2.1.x Due to Errors in Mapping Resonance Forms

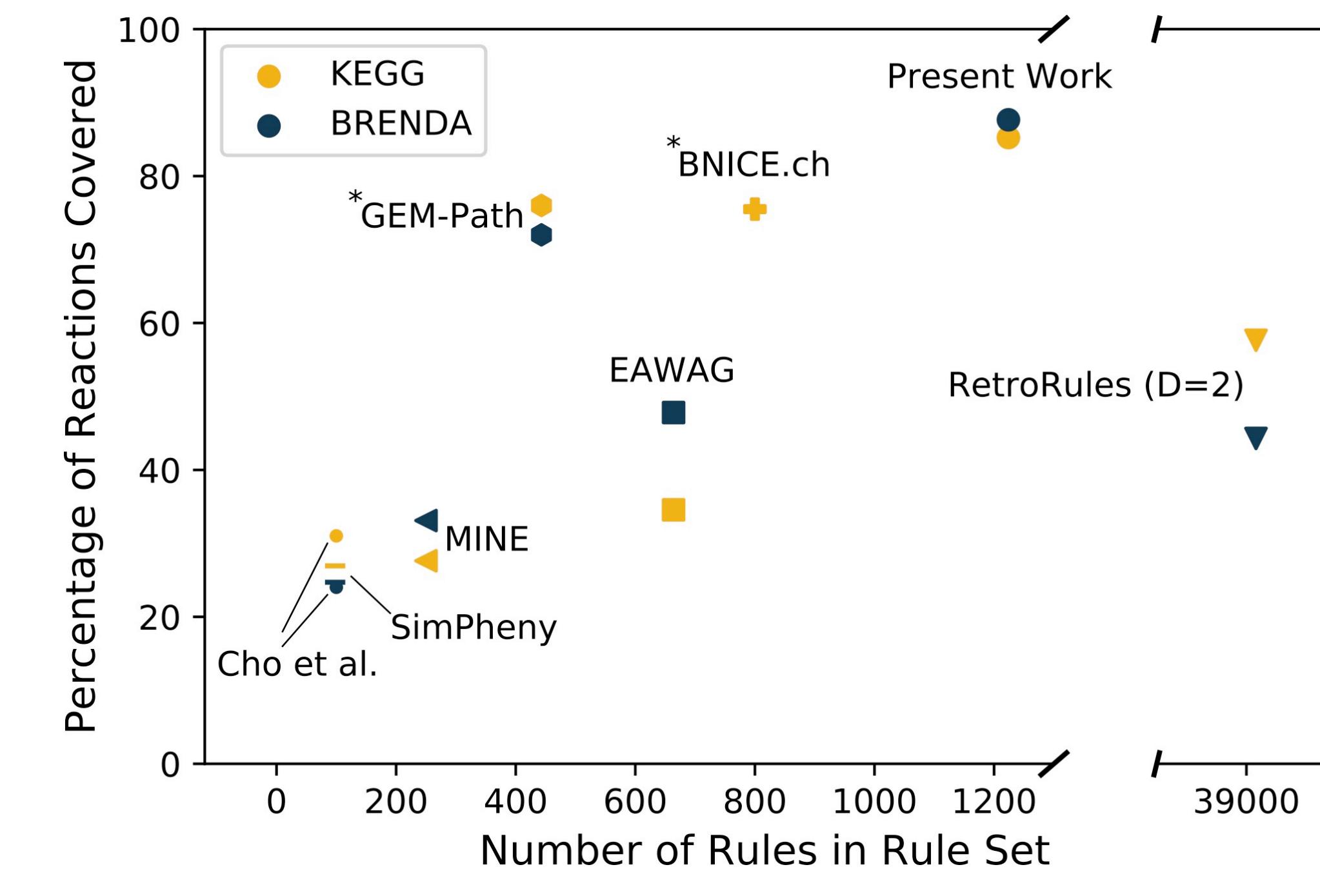
Pruning Process to Remove Redundant Reaction Rules



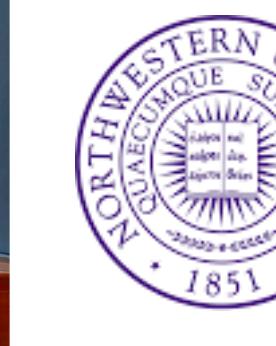
Coverage of Reaction Rules

Comparing Database Coverage vs Published Rule Sets

Using a subset of MetaCyc-derived and pruned rules (1224 rules each covering >1 known reactions), >85% of reactions in KEGG and BRENDA could be reproduced.



Acknowledgements



Northwestern University



LanzaTech capturing carbon fueling growth



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